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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/234,733	01/21/1999	MIN JIANG	9000-0030.10	5673

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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	29

DATE MAILED: 01/22/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/234,733	JIANG ET AL.
Examiner	**Art Unit**
Ja-Na Hines	1645

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED. (35 U.S.C. § 133)
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 October 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 44-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12 and 44-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
4) ☐ Interview Summary (PTO-413) Paper No(s).
5) ☐ Notice of Informal Patent Application (PTO-152)

DETAILED ACTION

Amendment Entry

1. The amendment filed October 8, 2002 has been entered. Claims 1, 3-4, 6, 44 and 46 have been amended. Claims 1-12 and 44-55 are under consideration in this office action.

Response to Arguments

2. Applicant's amendment filed October 8, 2002 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. The rejection of claims 1-12 and 44-55 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising SEQ ID NO:1 which encodes the amino acid sequence of SEQ ID NO:2 does not reasonably provide enablement for an isolated nucleic acid molecule encoding a polypeptide having at least 90% sequence identity to SEQ ID NO:2 or 5 is maintained because such amendments do not overcome the rejections.

As previously stated, applicants have not taught which residues of the sequence

immunogenic polypeptide having 90% sequence identity to SEQ ID NO 2 or 5. The

specification has not conceived of any other functionally equivalent polypeptides or sequences encoding an immunogenic polypeptide, there is no teaching of general tolerance to substitutions or where substitutions could be made. Thus the specification fails to enable the skilled artisan to envision the detailed chemical structure of the claimed structure of the claimed polypeptide. The skilled artisan would be forced into undue experimentation to make and use the instantly claimed invention.

The art teaches that replacement of a single amino acid residue may lead to both structural and functional changes in the biological activity of a protein. One of skill in the art would be reduced to merely randomly altering amino acids that would lead to unpredictable results regarding the functional activity of the immunogenic polypeptide. The art is replete with examples that even one amino acid change can lead to unpredictable changes in the biological activity of the protein, as stated in the previous office action. See also, Jobling et al., (1991) which teach a panel of single amino acid substitutions by oligonucleotide directed mutagenesis produces protein that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO:2 or 5 that can be varied by 10% and still achieve the desired polypeptide. The skilled artisan would have to discover what the appropriate additions, deletion and substitutions could be. This experimentation would require inventiveness beyond that expected skilled artisan.

substituted or inserted for the production of a polypeptide nor does the specificatio

provide guidance on how any location can be used to produce a stable polypeptide. There is no recitation of specific locations for deletions, substitutions, or insertions. In this regard, applicant has not enabled the scope of the invention as claimed for those amino acid sequences having at least 90% identity. Therefore, such undisclosed and unidentified amino acid and sequences, which result from insertions, deletions, or substitutions encompassed by the recited 90% identity, are not enabled for their scope. Therefore such undisclosed and unidentified amino acids, which result from these insertions, deletions or substitutions encompassed by the recited sequence having at least 90% sequence identity, are not enabled for their scope.

The specification does not provide a clear protocol by which the polypeptide comprising SEQ ID NO:5 or variants were isolated at the time the invention was made. The specification does not provide structural characterization of the complete open reading frame of the bacterial membrane, i.e., including a start codon. In the instant case, the classical start codon is missing. The specification alleges functionality, however polypeptides in the art are highly variant and all begin with a classic start codon. In view of the lack of evidence in the specification as filed, it is apparent that one skilled in the art would recognize that applicants were not in possession, at the time of filing the instant application, comprised in SEQ ID NO:5 or immunological variants. Absent characterization of the start codon, the genus of the polypeptides comprised in SEQ ID NO:5 or immunological variants is highly diverse and variant.

skill in the art. Such need for non-routine experimentation demonstrates that the

specification is not enabled for any asserted use or well-established use of a sequence encoding an immunogenic polypeptide having at least 90% identity to SEQ ID NO:2 or 5.

As stated above, there is no teaching of any other functionally equivalent polypeptides or sequences encoding an immunogenic polypeptide, there is no teaching of general tolerance to substitutions or where substitutions could be made; therefore the specification fails to enable the skilled artisan to envision the detailed chemical structure of the claimed structure of the claimed polypeptide and a skilled artisan would be forced into undue experimentation to make and use the instantly claimed invention.

In view of a specification which fails to provide guidance on how any amino acid can be substituted or inserted for the production of an immunogenic polypeptide and guidance on critical locations which cannot tolerate modifications, thereby allowing one to produce an immunogenic polypeptide having at least 90% sequence identity to SEQ ID NO: 2 or 5 without performing undue experimentation to achieve such results, the instant claims are not enabled and the rejection is maintained.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday [illegible] alternate Fridays

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines JH
January 13, 2003

LYNETTE R. SMITH
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER